

James & Esther King Biomedical Research Program

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*Oncological Sciences
H. Lee Moffitt Cancer Center & Research Institute*

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Research Project Grant
(5-year project)*

Project Title: Targeting AKT Pathway in Lung Cancer

Project Summary: Lung cancer is the leading cause of cancer-related death in the U.S.; 85-90 percent of such cases are associated with tobacco use. Current lung cancer non-surgical treatment is based on chemotherapy and radiation, and improvement in survival and quality of life has been observed. However, the disease is eventually refractory to these treatments. Therefore, there is a need to develop new therapies. Hyperactivation of Akt, an enzyme causing tumor development, is detected in more than 50 percent of lung cancer cases and is closely associated with chemo- and radio-resistance as well as EGFR and mTOR (key proteins involved in cancer cell growth) inhibitor resistance. Tobacco activates Akt, which is believed to mediate tobacco-induced lung cancer. We have identified two AKT inhibitors. API-2 is currently in clinical trial, and API-1 is a new small molecule inhibitor of Akt. These two inhibitors significantly decrease tumor growth and induce cancer cell death. Therefore, the goal of this project is to determine whether AKT inhibitors can be used as potential therapeutic and chemoprevention agents to inhibit AKT-dependant lung cancer cell growth, and as chemo- and radio-sensitizers to overcome the resistance of chemo-radiotherapy, EGFR inhibitors, and ineffectiveness of mTOR inhibitors. These investigations will provide important information on Akt inhibitor use for combinational clinical trials and chemoprevention of lung cancer.